REMARKS

Claims 13-31 are pending. Claims 14, 19-24, 26, 29, and 30 have been withdrawn as directed to non-elected inventions. Claims 15-18, 23, 24, and 27-30 have been canceled. Claims 13, 14, 19-22, and 31 have been amended. Claims 32-35 have been added. Reconsideration and allowance of Claims 13, 14, 19-22, 25, 26, and 31-35 in view of the above amendments and following remarks is respectfully requested.

The Provisional Double Patenting Rejection

Claims 13, 15-18, 25, 27, and 28 have been provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over Claims 41, 43-47, 57, 59, and 60 of copending Application No. 10/555,076. Applicants acknowledge the double patenting rejection and will file a terminal disclaimer in this or the '076 application on an indication of allowable subject matter.

The Rejection of Claims 13, 15-18, 25, 27, 28, and 31 Under 35 U.S.C. § 112, First Paragraph, Written Description

Claims 13, 15-18, 25, 27, 28, and 31 have been rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement. Withdrawal of the rejection is requested for the following reasons.

Claims 15-18, 27, and 28 have been canceled. Claims 13 and 31 have been amended. Claim 25 depends from Claim 13.

As amended, Claim 13 recites a method for enhancing glucose uptake into warm-blooded animal cells including administering an effective amount of pravastatin or pharmacologically acceptable salts or esters thereof. Claim 31 has been similarly amended and recites that administering an effective amount of pravastatin or pharmacologically acceptable salts or esters

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thereof includes administering pravastatin or pharmacologically acceptable salts or esters thereof in the presence of insulin.

Support for the amendment can be found throughout the application as originally filed. See, for example, page 11, lines 11-18.

Example 2 describes the glucose uptake enhancing action (in vivo) of pravastatin administered to live mice. See page 21, line 31 through page 25, line 14. The specification as originally filed, including Example 2, reasonably conveys to the skilled person that applicants had possession of the claimed invention, at the time of filing.

In view of the amendments to Claims 13 and 31, the specification as originally filed provides written descriptive support for the invention as now claimed. Applicants submit that the written description requirement has been met. Withdrawal of the rejection is requested.

The Rejection of Claims 13, 15-18, 25, 27, 28, and 31

Under 35 U.S.C. § 112, First Paragraph, Enablement

Claims 13, 15-18, 25, 27, 28, and 31 have been rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the enablement description requirement. Withdrawal of the rejection is requested for the following reasons.

Claims 15-18, 27, and 28 have been canceled. Claims 13 and 31 have been amended. Claim 25 depends from Claim 13.

As noted above, Claims 13 and 31 have been amended. As amended, Claim 13 recites a method for enhancing glucose uptake into warm-blooded animal cells including administering an effective amount of pravastatin or pharmacologically acceptable salts or esters thereof. Claim 31 has been similarly amended and recites that administering an effective amount of pravastatin or pharmacologically acceptable salts or esters thereof includes administering pravastatin or pharmacologically acceptable salts or esters thereof in the presence of insulin.

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Example 2 describes the glucose uptake enhancing action (in vivo) of pravastatin administered to live mice. See page 21, line 31 through page 25, line 14. The specification as originally filed, including Example 2, enables the skilled person to make and use the claimed invention without undue experimentation.

In view of the amendments to Claims 13 and 31, the invention as now claimed is enabled by the specification as originally filed. Applicants submit that the enablement requirement has been met. Withdrawal of the rejection is requested.

The Rejection of Claims 13, 15-18, 25, 27, and 28 Under 35 U.S.C. § 102(b)

Claims 13, 15-18, 25, 27, and 28 have been rejected under 35 U.S.C. § 102(b) as anticipated by (1) Paolisso et al., *European Journal of Clinical Pharmacology 40*(1):27-31 (the "Paolisso reference"), (2) Cingözbay et al., *Journal of International Medical Research 30*(1):21-25, January-February 2002 (the "Cingözbay reference"), (3) Freeman et al., *Circulation 103*:357-372, January 2001 (the "Freeman reference") and (4) Mangaloglu et al., *Metabolism 51*(4):409-418, April 2002 (the "Mangaloglu reference"). Withdrawal of the rejection is requested for the following reasons.

Claims 15-18, 27, and 28 have been canceled. Claim 13 has been amended. Claim 25 depends from Claim 13.

As amended, Claim 13 recites a method for enhancing glucose uptake into warm-blooded animal cells including administering an effective amount of pravastatin or pharmacologically acceptable salts or esters thereof.

According to the Examiner, each of the four cited references teaches the use of a HMG-CoA reductase inhibitor to treat insulin sensitivity (i.e., insulin resistance) and reduce glucose uptake in warm-blooded animal cells. The Examiner concludes that each of the cited references exactly describes the claimed invention. Applicants respectfully disagree.

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None of the cited references teaches enhancing glucose uptake with an HMG-CoA reductase inhibitor, particularly by administering pravastatin or pharmacologically acceptable salts or esters thereof, as now claimed.

The Paolisso reference describes that the administration of simvastatin in elderly non-insulin dependent diabetes patients exerts beneficial effects on lipid and glucose metabolism in various cells. The reference discloses that simvastatin treatment improves the action of insulin as demonstrated by stronger inhibition of hepatic glucose output and stimulation of both glucose disappearance rate and glucose metabolic rate. The reference fails to describe, teach, or suggest administering pravastatin or pharmacologically acceptable salts or esters thereof for any purpose.

The Cingözbay reference describes the effects of fluvastatin in the treatment of insulin sensitivity in patients with hyperlipidaemia. The reference discloses that anti-hyperlipidaemic treatment with fluvastatin increases insulin sensitivity (insulin resistance). The reference fails to describe, teach, or suggest administering pravastatin or pharmacologically acceptable salts or esters thereof for any purpose.

The Mangaloglu reference describes treatment with atorvastatin ameliorates hepatic very-low-density lipoprotein in an animal model of insulin resistance. The reference discloses that atorvastatin enhances hepatic insulin sensitivity (insulin resistance). The reference fails to describe, teach, or suggest administering pravastatin or pharmacologically acceptable salts or esters thereof for any purpose.

The Freeman reference describes the effect of pravastatin on the development of diabetes and discloses that there is an association between pravastatin therapy and a reduced risk of developing diabetes. The reference fails to disclose any relationship between pravastatin and glucose uptake. The Examiner notes that the reference teaches that the administration of

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"pravastatin may significantly influence selective tissue perfusion and thereby beneficially affect glucose and insulin transport."

In the same section of the reference, it states that pravastatin has a demonstrated effect on endothelial function and that impaired endothelial function has been shown to result in diminished capillary recruitment and to correlate with the degree of insulin resistance. The reference concludes the section by stating that by restoring endothelial function, pravastatin may significantly influence selective tissue perfusion and thereby beneficially affect glucose and insulin transport. The reference cautions that their "findings are generated from a post hoc analysis of WOSCOPS [West of Scotland Coronary Prevention Study] . . . . [and the] results should be treated as a hypothesis generating."

The Freeman reference discloses that there is an association between pravastatin therapy and a reduced risk of developing diabetes. However, the reference fails to disclose any relationship between pravastatin and glucose uptake. The citations in the reference noted by the Examiner that relate to endothelial function and the hypothesis that pravastatin therapy may reduce the propensity of subjects within WOSCOPS to develop diabetes do not bridge the gap between pravastatin and glucose uptake.

Applicants respectfully submit that the Freeman reference does not describe a method for enhancing glucose uptake by administering pravastatin. Accordingly, the reference is not anticipatory. Although the Freeman reference notes that there is an association between pravastatin therapy and a reduced risk of developing diabetes, the reference fails to teach, suggest, provide any motivation to make, or otherwise render the claimed invention obvious.

In summary, because the cited references fail to exactly describe the invention as now claimed, the references are not anticipatory. Withdrawal of the rejections is respectfully requested. Furthermore, because the cited references fail to teach, suggest, provide any

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motivation to make, or otherwise render obvious the invention as now claimed, the claimed invention is nonobvious and patentable over the cited references.

The Rejection of Claim 31 Under 35 U.S.C. § 103(a)

Claim 31 has been rejected under 35 U.S.C. § 103(a) as unpatentable over the Paolisso, Cingözbay, Freeman, or Mangaloglu references, in view of U.S. Patent No. 5,643,868, issued to Weiner et al. Withdrawal of the rejection is requested for the following reasons.

Claim 31 has been amended. Claim 31 depends from Claim 13. As amended, Claim 31 recites that administering an effective amount of pravastatin or pharmacologically acceptable salts or esters thereof includes administering pravastatin or pharmacologically acceptable salts or esters thereof in the presence of insulin.

The teachings of the Paolisso, Cingözbay, Freeman, and Mangaloglu references are noted above in regard to the rejection of Claims 13, 15-18, 25, 27, and 28. The deficiencies of the teaching of these references with regard to administering pravastatin or pharmacologically acceptable salts or esters thereof are not cured by the teaching of the Weiner reference.

The Weiner reference is directed to methods for treating or preventing a disease in mammals having the characteristics of Type 1 diabetes. The method includes the step of administering insulin or disease suppressive fragments of insulin or analogs to the mammals. The reference fails to describe, teach, or suggest administering pravastatin or pharmacologically acceptable salts or esters thereof for any purpose.

As acknowledged by the Examiner the Paolisso, Cingözbay, Freeman, and Mangaloglu references do not teach the administration of insulin. These references do not teach the administration of pravastatin or pharmacologically acceptable salts or esters thereof for enhancing glucose uptake into warm-blooded animal cells. Neither does the Weiner reference. Therefore, the combined teachings of the cited references fail to teach every limitation of the

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claimed invention. The cited references simply fail to teach, suggest, or provide any motivation to arrive at the invention as now claimed: a method for enhancing glucose uptake that includes administering an effective amount of pravastatin or pharmacologically acceptable salts or esters thereof in the presence of insulin.

Because the cited references, either alone or in any combination, fail to teach, remotely suggest, provide any motivation to make, or otherwise render obvious the invention as now claimed, the claimed invention is nonobvious and patentable over the cited reference. Withdrawal of the rejection is requested.

New Claims 32-35

Dependent Claims 32-35 have been added. Claim 32 depends from Claim 13 and recites the further administration of an effective amount of a second HMG-CoA reductase inhibitor. Claim 33 depends from Claim 32 and recites that the second HMG-CoA reductase inhibitor is selected from lovastatin, simvastatin, fluvastatin, cerivastatin, atorvastatin, pitavastatin, and rosuvastatin. Claim 34 depends from Claim 31 and recites the further administration of an effective amount of a second HMG-CoA reductase inhibitor. Claim 35 depends from Claim 34 and recites that the second HMG-CoA reductase inhibitor is selected from lovastatin, simvastatin, fluvastatin, cerivastatin, atorvastatin, pitavastatin, and rosuvastatin.

Support for Claims 32-35 can be found throughout the application as originally filed. See, for example, page 14, lines 10-16 and the Examples section, page 19, line 22 through page 25, line 31.

Co-administration of therapeutic drug compounds is well known to those of skill in the art. Applicants submit that the specification as originally filed, including Example 2, reasonably conveys to the skilled person that applicants had possession of the invention of Claims 32-35, at the time of filing. Applicants further submit that the specification as originally filed, including

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Example 2, enables the skilled person to make and use the invention of Claims 32-35 without undue experimentation.

Rejoinder of Withdrawn Claims 14, 19-22, and 26

Independent Claims 14, and 19-22 have been amended to conform to amended Claim 13. Rejoinder of withdrawn Claims 14, 19-22, and 26 is requested.

CONCLUSION

In view of the above amendments and the foregoing remarks, applicants believe that Claims 13, 14, 19-22, 25, 26, and 31-35 are in condition for allowance. If any issues remain that may be expeditiously addressed by a telephone interview, the Examiner is encouraged to telephone applicants' attorney at 206.695.1755.

Respectfully submitted,

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